



prekallikrein deficiency

Prekallikrein deficiency is a blood condition that usually causes no health problems. In people with this condition, blood tests show a prolonged activated partial thromboplastin time (PTT), a result that is typically associated with bleeding problems; however, bleeding problems generally do not occur in prekallikrein deficiency. The condition is usually discovered when blood tests are done for other reasons.

A few people with prekallikrein deficiency have experienced health problems related to blood clotting such as heart attack, stroke, a clot in the deep veins of the arms or legs (deep vein thrombosis), nosebleeds, or excessive bleeding after surgery. However, these are common problems in the general population, and most affected individuals have other risk factors for developing them, so it is unclear whether their occurrence is related to prekallikrein deficiency.

Frequency

The prevalence of prekallikrein deficiency is unknown. Approximately 80 affected individuals in about 30 families have been described in the medical literature. Because prekallikrein deficiency usually does not cause any symptoms, researchers suspect that most people with the condition are never diagnosed.

Genetic Changes

Prekallikrein deficiency is caused by mutations in the *KLKB1* gene, which provides instructions for making a protein called prekallikrein. This protein, when converted to an active form called plasma kallikrein in the blood, is involved in the early stages of blood clotting. Plasma kallikrein plays a role in a process called the intrinsic coagulation pathway (also called the contact activation pathway). This pathway turns on (activates) proteins that are needed later in the clotting process. Blood clots protect the body after an injury by sealing off damaged blood vessels and preventing further blood loss.

The *KLKB1* gene mutations that cause prekallikrein deficiency reduce or eliminate functional plasma kallikrein, which likely impairs the intrinsic coagulation pathway. Researchers suggest that this lack (deficiency) of functional plasma kallikrein protein does not generally cause any symptoms because another process called the extrinsic coagulation pathway (also known as the tissue factor pathway) can compensate for the impaired intrinsic coagulation pathway.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal

recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- congenital prekallikrein deficiency
- Fletcher factor deficiency
- Fletcher trait
- PKK deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Prekallikrein deficiency
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0272339/>

Other Diagnosis and Management Resources

- Massachusetts General Hospital Laboratory Handbook: Prekallikrein
<http://mghlabtest.partners.org/coagbook/CO002600.htm>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Bleeding Disorders
<https://medlineplus.gov/bleedingdisorders.html>

Genetic and Rare Diseases Information Center

- Prekallikrein deficiency, congenital
<https://rarediseases.info.nih.gov/diseases/4477/prekallikrein-deficiency-congenital>

Educational Resources

- Disease InfoSearch: Prekallikrein deficiency
<http://www.diseaseinfosearch.org/Prekallikrein+deficiency/9145>
- MalaCards: prekallikrein deficiency, congenital
http://www.malacards.org/card/prekallikrein_deficiency_congenital
- Orphanet: Congenital prekallikrein deficiency
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=749

Patient Support and Advocacy Resources

- National Blood Clot Alliance
<https://www.stoptheclot.org/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28prekallikrein+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>

OMIM

- PREKALLIKREIN DEFICIENCY
<http://omim.org/entry/612423>

Sources for This Summary

- François D, Trigui N, Leterreux G, Flaujac C, Horellou MH, Mazaux L, Vignon D, Conard J, de Mazancourt P. Severe prekallikrein deficiencies due to homozygous C529Y mutations. *Blood Coagul Fibrinolysis*. 2007 Apr;18(3):283-6.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17413767>
- Girolami A, Allemand E, Bertozzi I, Candeo N, Marun S, Girolami B. Thrombotic events in patients with congenital prekallikrein deficiency: a critical evaluation of all reported cases. *Acta Haematol*. 2010;123(4):210-4. doi: 10.1159/000313361. Epub 2010 Apr 27.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20424433>
- Girolami A, Scarpato P, Candeo N, Lombardi AM. Congenital prekallikrein deficiency. *Expert Rev Hematol*. 2010 Dec;3(6):685-95. doi: 10.1586/ehm.10.69. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21091145>
- Nakao T, Yamane T, Katagami T, Shiota M, Izumi Y, Samori T, Hino M, Iwao H. Severe prekallikrein deficiency due to a homozygous Trp499Stop nonsense mutation. *Blood Coagul Fibrinolysis*. 2011 Jun;22(4):337-9. doi: 10.1097/MBC.0b013e3283444ddb.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21415712>

- Quail MT. Prekallikrein deficiency. J Pediatr Oncol Nurs. 2013 Jul-Aug;30(4):198-204. doi: 10.1177/1043454213487436. Epub 2013 Apr 29. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23629422>
 - Wynne Jones D, Russell G, Allford SL, Burdon K, Hawkins GA, Bowden DW, Minaee S, Mumford AD. Severe prekallikrein deficiency associated with homozygosity for an Arg94Stop nonsense mutation. Br J Haematol. 2004 Oct;127(2):220-3.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15461630>
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